

Title (en)  
HUMAN FGF RECEPTOR AND BETA-KLOTHO BINDING PROTEINS

Title (de)  
HUMANER FGF-REZEPTOR UND BETA-KLOTHO-BINDEPROTEINE

Title (fr)  
RÉCEPTEUR FGF HUMAIN ET PROTÉINES DE LIAISON DE BÊTA-KLOTHO

Publication  
**EP 3670534 A2 20200624 (EN)**

Application  
**EP 19200863 A 20110413**

Previously filed application  
PCT/US2011/032333 20110413 WO

Priority

- US 32469110 P 20100415
- US 39285910 P 20101013
- EP 11715374 A 20110413
- US 2011032333 W 20110413

Abstract (en)

The present invention provides compositions and methods relating to or derived from antigen binding proteins and antigen binding protein-FGF21 fusions that specifically bind to  $\beta$ -Klotho, or  $\beta$ -Klotho and one or more of FGFR1c, FGFR2c, FGFR3c, and FGFR4. In some embodiments the antigen binding proteins and antigen binding protein-FGF21 fusions induce FGF21-like signaling. In some embodiments, an antigen binding protein or antigen binding protein-FGF21 fusion antigen binding component is a fully human, humanized, or chimeric antibody, binding fragments and derivatives of such antibodies, and polypeptides that specifically bind to  $\beta$ -Klotho, or  $\beta$ -Klotho and one or more of FGFR1c, FGFR2c, FGFR3c, and FGFR4. Other embodiments provide nucleic acids encoding such antigen binding proteins and antigen binding protein-FGF21 fusions, and fragments and derivatives thereof, and polypeptides, cells comprising such polynucleotides, methods of making such antigen binding proteins and antigen binding protein-FGF21 fusions, and fragments and derivatives thereof, and polypeptides, and methods of using such antigen binding proteins and antigen binding protein-FGF21 fusions, fragments and derivatives thereof, and polypeptides, including methods of treating or diagnosing subjects suffering from type 2 diabetes, obesity, NASH, metabolic syndrome and related disorders or conditions.

IPC 8 full level  
**C07K 16/28** (2006.01); **A61K 39/395** (2006.01); **A61P 1/16** (2006.01); **A61P 3/00** (2006.01); **A61P 3/04** (2006.01); **A61P 3/06** (2006.01); **A61P 3/10** (2006.01); **A61P 9/00** (2006.01); **A61P 43/00** (2006.01); **C07K 16/40** (2006.01)

CPC (source: EP US)  
**A61K 39/3955** (2013.01 - US); **A61P 1/16** (2018.01 - EP); **A61P 3/00** (2018.01 - EP); **A61P 3/04** (2018.01 - EP); **A61P 3/06** (2018.01 - EP); **A61P 3/10** (2018.01 - EP); **A61P 9/00** (2018.01 - EP); **A61P 43/00** (2018.01 - EP); **C07K 16/2863** (2013.01 - EP US); **C07K 16/40** (2013.01 - EP US); **C07K 2317/21** (2013.01 - EP US); **C07K 2317/31** (2013.01 - EP US); **C07K 2317/32** (2013.01 - EP US); **C07K 2317/75** (2013.01 - EP US); **C07K 2317/92** (2013.01 - EP US); **C07K 2319/75** (2013.01 - EP US)

Citation (applicant)

- US 61324691 P
- US 61392859 P
- US 6846634 B1 20050125 - TOMLINSON IAN [GB], et al
- US 6696245 B2 20040224 - WINTER GREG [GB], et al
- US 2005202512 A1 20050915 - TOMLINSON IAN [GB], et al
- US 2004202995 A1 20041014 - DE WILDT RUDOLF MARIA THEODORA [GB], et al
- US 2004038291 A2 20040226 - TOMLINSON IAN [GB], et al
- US 2004009507 A1 20040115 - WINTER GREGORY PAUL [GB], et al
- US 2003039958 A1 20030227 - HOLT LUCY JESSICA [GB], et al
- US 6054297 A 20000425 - CARTER PAUL J [US], et al
- US 5886152 A 19990323 - NAKATANI TOMOYUKI [JP], et al
- US 5877293 A 19990302 - ADAIR JOHN ROBERT [GB], et al
- US 4816567 A 19890328 - CABILLY SHMUEL [US], et al
- US 6180370 B1 20010130 - QUEEN CARY L [US], et al
- US 5693762 A 19971202 - QUEEN CARY L [US], et al
- US 5693761 A 19971202 - QUEEN CARY L [US], et al
- US 5585089 A 19961217 - QUEEN CARY L [US], et al
- US 5530101 A 19960625 - QUEEN CARY L [US], et al
- WO 9633735 A1 19961031 - CELL GENESYS INC [US]
- WO 9402602 A1 19940203 - CELL GENESYS INC [US]
- US 5545807 A 19960813 - SURANI AZIM M [GB], et al
- US 6713610 B1 20040330 - KUCHERLAPATI RAJU [US], et al
- US 6673986 B1 20040106 - KUCHERLAPATI RAJU [US], et al
- US 6162963 A 20001219 - KUCHERLAPATI RAJU [US], et al
- US 6300129 B1 20011009 - LONBERG NILS [US], et al
- US 6255458 B1 20010703 - LONBERG NILS [US], et al
- US 5877397 A 19990302 - LONBERG NILS [US], et al
- US 5874299 A 19990223 - LONBERG NILS [US], et al
- US 5545806 A 19960813 - LONBERG NILS [US], et al
- WO 9110741 A1 19910725 - CELL GENESYS INC [US]
- WO 9004036 A1 19900419 - MEDICAL RES COUNCIL [GB], et al
- EP 0546073 A1 19930616 - GENPHARM INT [US]
- EP 0546073 A1 19930616 - GENPHARM INT [US]
- US 5569825 A 19961029 - LONBERG NILS [US], et al
- US 5625126 A 19970429 - LONBERG NILS [US], et al
- US 5633425 A 19970527 - LONBERG NILS [US], et al
- US 5789650 A 19980804 - LONBERG NILS [US], et al

- US 5661016 A 19970826 - LONBERG NILS [US], et al
- US 5814318 A 19980929 - LONBERG NILS [US], et al
- US 5770429 A 19980623 - LONBERG NILS [US], et al
- WO 9301227 A1 19930121 - UNIV MASSACHUSETTS [US]
- WO 9222646 A1 19921223 - DNX CORP [US]
- WO 9203918 A1 19920319 - GENPHARM INT [US]
- WO 9824893 A2 19980611 - ABGENIX INC [US]
- WO 9910494 A2 19990304 - GENENTECH INC [US]
- US 4751180 A 19880614 - COUSENS LAWRENCE S [US], et al
- US 4935233 A 19900619 - BELL LESLIE D [GB], et al
- US 5011912 A 19910430 - HOPP THOMAS P [US], et al
- WO 9310151 A1 19930527 - IMMUNEX CORP [US]
- US 5426048 A 19950620 - GEARING DAVID P [US]
- US 5262522 A 19931116 - GEARING DAVID P [US]
- US 5457035 A 19951010 - BAUM PETER R [US], et al
- WO 9410308 A1 19940511 - IMMUNEX CORP [US]
- WO 0009560 A2 20000224 - ABGENIX INC [US]
- WO 8705330 A1 19870911 - BERGH MICHEL LOUIS EUGENE, et al
- WO 9215673 A1 19920917 - UNIV GEORGIA RES FOUND [US]
- WO 9507463 A1 19950316 - UNIV COLUMBIA [US], et al
- WO 9814605 A1 19980409 - UNIV LOMA LINDA [US]
- WO 9826277 A2 19980618 - PROLUME LTD [US], et al
- WO 9949019 A2 19990930 - PROLUME LTD [US], et al
- US 5292658 A 19940308 - CORMIER MILTON J [US], et al
- US 5418155 A 19950523 - CORMIER MILTON J [US], et al
- US 5683888 A 19971104 - CAMPBELL ANTHONY KEITH [GB]
- US 5741668 A 19980421 - WARD WILLIAM W [US], et al
- US 5777079 A 19980707 - TSIEN ROGER Y [US], et al
- US 5804387 A 19980908 - CORMACK BRENDAN P [US], et al
- US 5874304 A 19990223 - ZOLOTUKHIN SERGEI [US], et al
- US 5876995 A 19990302 - BRYAN BRUCE [US]
- US 5925558 A 19990720 - TSIEN ROGER Y [US], et al
- US 4946778 A 19900807 - LADNER ROBERT C [US], et al
- US 4399216 A 19830816 - AXEL RICHARD [US], et al
- US 4912040 A 19900327 - KAUFMAN RANDAL J [US], et al
- US 4740461 A 19880426 - KAUFMAN RANDAL J [US]
- US 4959455 A 19900925 - CLARK STEVEN C [US], et al
- US 6270964 B1 20010807 - MICHNICK STEPHEN WILLIAM WATSO [CA], et al
- US 4965195 A 19901023 - NAMEN ANTHONY E [US], et al
- EP 0367566 A1 19900509 - IMMUNEX CORP [US]
- US 4968607 A 19901106 - DOWER STEVEN K [US], et al
- EP 0460846 A1 19911211 - IMMUNEX CORP [US]
- US 9401875 W 19940222
- US 9300829 W 19930205
- US 3773919 A 19731120 - BOSWELL G, et al
- EP 0058481 A1 19820825 - ICI PLC [GB]
- EP 0133988 A2 19850313 - HOECHST AG [DE]
- EP 0036676 A1 19810930 - UNIV CALIFORNIA [US]
- EP 0088046 A2 19830907 - CIBA GEIGY AG [CH]
- EP 0143949 A1 19850612 - TERUMO CORP [JP]
- US 75962096 A 19961203
- WO 0076310 A1 20001221 - ABGENIX INC [US], et al
- ITOH ET AL., TREND GENET., vol. 20, 2004, pages 563 - 69
- KHARITONENKOV ET AL., BIODRUGS, vol. 22, 2008, pages 37 - 44
- KUROSU ET AL., J. BIOL. CHEM., vol. 282, 2007, pages 26687 - 26695
- OGAWA ET AL., PROC. NATL. ACAD. SCI. USA, vol. 104, 2007, pages 7432 - 7437
- KHARITONENKOV ET AL., J. CELL PHYSIOL., vol. 215, 2008, pages 1 - 7
- KORNDORFER ET AL., PROTEINS: STRUCTURE, FUNCTION, AND BIOINFORMATICS, vol. 53, no. 1, 2003, pages 121 - 129
- ROQUE ET AL., BIOTECHNOL. PROG., vol. 20, 2004, pages 639 - 654
- CHOITHIA ET AL., NATURE, vol. 334, 1989, pages 544 - 883
- HOOGENBOOM ET AL., J. MOL. BIOL., vol. 222, 1991, pages 581
- CHOTHIALESK, J. MOL. BIOL., vol. 196, 1987, pages 901 - 917
- LANDSCHULZ ET AL., SCIENCE, vol. 242, 1988, pages 1759 - 1536
- HUSTON ET AL., PROC. NATL. ACAD. SCI. USA, vol. 85, 1988, pages 5879 - 83
- JAKOBOVITS ET AL., PROC. NATL. ACAD. SCI. USA, vol. 90, 1993, pages 2551 - 2555
- POLJAK ET AL., STRUCTURE, vol. 2, 1994, pages 1121 - 23
- SONGSIVILAILACHMANN, CLIN. EXP. IMMUNOL., vol. 79, 1990, pages 315 - 321
- KOSTELNY ET AL., J. IMMUNOL., vol. 148, 1992, pages 1547 - 1553
- GRAHAM ET AL., VIROLOGY, vol. 52, 1973, pages 456
- KRIANGKUM ET AL., BIOMOL. ENG., vol. 18, 2001, pages 31 - 108
- KIRKLAND ET AL., J. IMMUNOL., vol. 137, 1986, pages 3614 - 3619
- CHU ET AL., GENE, vol. 13, 1981, pages 197
- STAHLI ET AL., METHODS IN ENZYMOLOGY, vol. 9, 1983, pages 242 - 253
- MOREL ET AL., MOLEC. IMMUNOL., vol. 25, 1988, pages 7 - 15
- CHEUNG ET AL., VIROLOGY, vol. 176, 1990, pages 546 - 552
- MOLDENHAUER ET AL., SCAND. J. IMMUNOL., vol. 32, 1990, pages 77 - 82
- CARILLO ET AL., SIAMJ. APPLIED MATH., vol. 48, 1988, pages 1073
- JAKOBOVITS ET AL., NATURE, vol. 362, 1993, pages 255 - 258
- LONBERG ET AL., NATURE, vol. 368, 1994, pages 856 - 859
- GRIBSKOV ET AL., PROC. NAT. ACAD. SCI., vol. 84, 1987, pages 4355 - 4358
- DEVEREUX ET AL., NUCL. ACID RES., vol. 12, 1984, pages 387
- DAYHOFF ET AL., ATLAS OF PROTEIN SEQUENCE AND STRUCTURE, vol. 5, 1978, pages 345 - 352
- HENIKOFF ET AL., PROC. NATL. ACAD. SCI. U.S.A., vol. 89, 1992, pages 10915 - 10919

- NEEDLEMAN ET AL., J. MOL. BIOL., vol. 48, 1970, pages 443 - 453
- "GenBank", Database accession no. 783864
- MORRISON, PROC. NATL. ACAD. SCI. USA, vol. 81, 1985, pages 6851 - 6855
- JONES ET AL., NATURE, vol. 321, 1986, pages 522 - 525
- RIECHMANN ET AL., NATURE, vol. 332, 1988, pages 323 - 27
- BRUGGERMANN ET AL., YEAR IN IMMUNOL., vol. 7, no. 33, 1993
- LONBERGHUSZAR, INTERN. REV. IMMUNOL., vol. 13, 1995, pages 65 - 93
- HARDINGLONBERG, ANN. NY ACAD. SCI., vol. 764, 1995, pages 536 - 546
- TAYLOR ET AL., NUCLEIC ACIDS RESEARCH, vol. 20, 1992, pages 6287 - 6295
- CHEN ET AL., INTERNATIONAL IMMUNOLOGY, vol. 5, 1993, pages 647 - 656
- TUAILLON ET AL., J. IMMUNOL., vol. 152, 1994, pages 2912 - 2920
- LONBERG, HANDBOOK OF EXP. PHARMACOLOGY, vol. 113, 1994, pages 49 - 101
- TAYLOR ET AL., INTERNATIONAL IMMUNOLOGY, vol. 6, 1994, pages 579 - 591
- HARDINGLONBERG, ANN. N.YACAD. SCI., vol. 764, 1995, pages 536 - 546
- FISHWILD ET AL., NATURE BIOTECHNOLOGY, vol. 14, 1996, pages 845 - 851
- MENDEZ ET AL., NATURE GENETICS, vol. 15, 1997, pages 146 - 156
- KYTE ET AL., J. MOL. BIOL., vol. 157, 1982, pages 105 - 131
- MOULTCHOU ET AL., CURR. OP. IN BIOTECH., vol. 7, 1974, pages 422 - 427
- BIOCHEM., vol. 13, pages 222 - 245
- CHOU ET AL., BIOCHEMISTRY, vol. 113, 1974, pages 211 - 222
- CHOU ET AL., ADV. ENZYMOL. RELAT. AREAS MOL. BIOL., vol. 47, 1978, pages 45 - 148
- CHOU ET AL., ANN. REV. BIOCHEM., vol. 47, 1979, pages 251 - 276
- CHOU ET AL., BIOPHYS. J., vol. 26, 1979, pages 367 - 384
- HOLM ET AL., NUCL. ACID. RES., vol. 27, 1999, pages 244 - 247
- BRENNER ET AL., CURR. OP. STRUCT. BIOL., vol. 7, 1997, pages 369 - 376
- JONES, CURR. OPIN. STRUCT. BIOL., vol. 7, 1997, pages 377 - 387
- SIPPL ET AL., STRUCTURE, vol. 4, 1996, pages 15 - 19
- BOWIE ET AL., SCIENCE, vol. 253, 1991, pages 164 - 170
- GRIBSKOV ET AL., METH. ENZYM., vol. 183, 1990, pages 146 - 159
- THOMSEN ET AL., PROC. NATL. ACAD. U.S.A., vol. 81, 1984, pages 659 - 663
- THORNTON ET AL., NATURE, vol. 354, 1991, pages 105
- FAUCHERE, ADV. DRUG RES., vol. 15, 1986, pages 29
- VEBERFREIDINGER, TINS, 1985, pages 392
- EVANS ET AL., J. MED. CHEM., vol. 30, 1987, pages 1229
- RIZOGIERASCH, ANN. REV. BIOCHEM., vol. 61, 1992, pages 387
- HOPP ET AL., BIO/TECHNOLOGY, vol. 6, 1988, pages 1204
- ASHKENAZI ET AL., PROC. NATL. ACAD. SCI. USA, vol. 88, 1991, pages 10535
- BYRN ET AL., NATURE, vol. 344, 1990, pages 677
- HOLLENBAUGH ET AL.: "Construction of Immunoglobulin Fusion Proteins", CURRENT PROTOCOLS IN IMMUNOLOGY, 1992
- BAUM ET AL., EMBO J., vol. 13, 1994, pages 3992 - 4001
- HOPPE ET AL., FEBS LETTERS, vol. 344, 1994, pages 191
- FANSLow ET AL., SEMIN. IMMUNOL., vol. 6, 1994, pages 267 - 278
- APLINWRISTON, CRC CRIT. REV. BIOCHEM., 1981, pages 259 - 306
- HAKIMUDDIN ET AL., ARCH. BIOCHEM. BIOPHYS., vol. 259, 1987, pages 52
- EDGE ET AL., ANAL. BIOCHEM., vol. 118, 1981, pages 131
- THOTAKURA ET AL., METH. ENZYMOL., vol. 138, 1987, pages 350
- DUSKIN ET AL., J. BIOL. CHEM., vol. 257, 1982, pages 3105
- CHALFIE ET AL., SCIENCE, vol. 263, 1994, pages 802 - 805
- "Genbank", Database accession no. U55762
- "Biotechniques", vol. 24, 1998, BFP, QUANTUM BIOTECHNOLOGIES, INC., pages: 462 - 471
- HEIM ET AL., CURR. BIOL., vol. 6, 1996, pages 178 - 182
- ICHIKI ET AL., J. IMMUNOL., vol. 150, 1993, pages 5408 - 5417
- HUSTON ET AL., PROC. NATL. ACAD. SCI. U.S.A., vol. 85, 1988, pages 5879 - 2607
- KOHLERMILSTEIN, NATURE, vol. 256, 1975, pages 495
- KORTT ET AL., PROT. ENG., vol. 10, 1997, pages 423
- DE GRAAF ET AL., METHODS MOL BIOL., vol. 178, 2002, pages 379 - 387
- LANTO ET AL., METHODS MOL. BIOL., vol. 178, 2002, pages 303 - 316
- BLOOM ET AL., PROTEIN SCIENCE, vol. 6, 1997, pages 407
- MARKS ET AL., BIOTECHNOLOGY, vol. 10, 1992, pages 779
- YAMAMOTO ET AL., CELL, vol. 22, 1980, pages 787 - 797
- HARLOWLANE: "Antibodies: A Laboratory Manual", 1988, COLD SPRING HARBOR LABORATORY PRESS
- BIANCHIMCGREW, BIOTECH. BIOTECHNOL. BIOENG., vol. 84, 2003, pages 439 - 44
- "Remington's Pharmaceutical Sciences", vol. 185, 1990, MACK PUBLISHING COMPANY
- WAGNER ET AL., PROC. NATL. ACAD. SCI. U.S.A., vol. 78, 1981, pages 1444 - 1445
- PRINSTER ET AL., NATURE, vol. 296, 1982, pages 39 - 42
- VILLA-KAMAROFF ET AL., PROC. NATL. ACAD. SCI. U.S.A., vol. 75, 1978, pages 3727 - 3731
- DEBOER ET AL., PROC. NATL. ACAD. SCI. U.S.A., vol. 80, 1983, pages 21 - 25
- GROSSCHEDL ET AL., CELL, vol. 38, 1984, pages 647 - 658
- ORNITZ ET AL., COLD SPRING HARBOR SYMP. QUANT. BIOL., vol. 50, 1986, pages 399 - 409
- MACDONALD, HEPATOLOGY, vol. 7, 1987, pages 425 - 515
- MOGRAM ET AL., NATURE, vol. 314, 1985, pages 283 - 286
- ALEXANDER ET AL., MOL. CELL. BIOL., vol. 7, 1987, pages 1436 - 1444
- KOLLIAS ET AL., CELL, vol. 46, 1986, pages 485 - 495
- PINKERT ET AL., GENES AND DEVEL., vol. 1, 1987, pages 161 - 171
- KRUMLAUF ET AL., MOL. CELL. BIOL., vol. 5, 1985, pages 1639 - 1648
- HAMMER ET AL., SCIENCE, vol. 253, 1987, pages 53 - 58
- READHEAD ET AL., CELL, vol. 48, 1987, pages 703 - 712
- MASON ET AL., SCIENCE, vol. 234, 1986, pages 1372 - 1378
- COSMAN ET AL., NATURE, vol. 312, 1984, pages 768
- TIJSSSEN: "Practice and Theory of Enzyme Immunoassays", vol. 15, 1993, JOHN WILEY & SONS
- JALKANEN ET AL., J. CELL BIOL., vol. 105, 1987, pages 3087 - 3096
- JALKANEN ET AL., J. CELL. BIOL., vol. 101, 1985, pages 976 - 985
- SIDMAN ET AL., BIOPOLYMERS, vol. 2, 1983, pages 547 - 556

- LANGER ET AL., J. BIOMED. MATER. RES., vol. 15, 1981, pages 167 - 277
- LANGER, CHEM. TECH., vol. 12, 1982, pages 98 - 105
- EPPSTEIN ET AL., PROC. NATL. ACAD. SCI. U.S.A., vol. 82, 1985, pages 3688 - 3692
- INVEST. OPHTHALMOL VIS SCI, vol. 43, 2002, pages 3292 - 3298
- PROC. NATL. ACAD. SCIENCES USA, vol. 103, 2006, pages 3896 - 3901
- KEARNEY ET AL., J. IMMUNOL., vol. 123, 1979, pages 1548 - 1550
- NANEVICZ ET AL., J. BIOL. CHEM., vol. 270, no. 37, 1995, pages 21619 - 21625
- ZUPNICK ET AL., J. BIOL. CHEM., vol. 281, no. 29, 2006, pages 20464 - 20473
- WU ET AL., J. BIOL. CHEM., vol. 283, 2008, pages 33304 - 33309

Designated contracting state (EPC)

AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HR HU IE IS IT LI LT LU LV MC MK MT NL NO PL PT RO RS SE SI SK SM TR

Designated extension state (EPC)

BA ME

DOCDB simple family (publication)

**WO 2011130417 A2 20111020; WO 2011130417 A3 20120308;** AU 2011239689 A1 20121108; CA 2796055 A1 20111020; EP 2558497 A2 20130220; EP 3670534 A2 20200624; EP 3670534 A3 20200909; JP 2013523184 A 20130617; MX 2012011986 A 20130305; US 2013129725 A1 20130523; US 9517264 B2 20161213

DOCDB simple family (application)

**US 2011032333 W 20110413;** AU 2011239689 A 20110413; CA 2796055 A 20110413; EP 11715374 A 20110413; EP 19200863 A 20110413; JP 2013505101 A 20110413; MX 2012011986 A 20110413; US 201113641041 A 20110413